**NCI ALLIANCE FOR NANOTECHNOLOGY IN CANCER**
**CANCER NANOTECHNOLOGY PLATFORM PARTNERSHIPS**

**FACT SHEET**

**OCTOBER 2005**

For the past seven years, the National Cancer Institute (NCI) has taken the lead in integrating nanotechnology into biomedical research through a variety of programs. The results of these efforts have demonstrated clearly that combining development efforts in nanotechnology and cancer research will have a profound, transformative effect on how we prevent, diagnose, and treat cancer.

To capitalize on the promise of nanotechnology in cancer, the NCI launched the Alliance for Nanotechnology in Cancer in September 2004. The Alliance, built on a strong foundation of science and scientific accomplishment, is a comprehensive, systematized initiative encompassing the public and private sectors. It is designed to accelerate the application of nanotechnology to the major challenges in clinical oncology and basic cancer research.

The Alliance has four major components:

- **Centers of Cancer Nanotechnology Excellence (CCNEs)** are seven hubs funded over 5 years to develop and apply nanotechnology and nanoscience solutions to the diagnosis and treatment of cancer. These awards were announced on October 3, 2005 (see press release). Funding for the first year of this program will total $26.3 million.
- **Cancer Nanotechnology Platform Partnerships** are tightly focused programs designed to develop the technologies to underpin new products in six key programmatic areas: molecular imaging and early detection, *in vivo* imaging, reporters of efficacy (e.g., real-time assessment of treatment), multifunctional therapeutics, prevention and control, and research enablers (opening new pathways for research). These 12, 5-year R01 awards were announced on October 17, 2005. The first-year funding on these awards will total $7 million.
- **The Nanotechnology Characterization Laboratory (NCL)**, (http://ncl.cancer.gov/), established at NCI's Frederick, Maryland, facility in 2004, performs analytical tests to guide the research community; support regulatory decisions; and help identify and monitor environmental, health, and safety ramifications of nanotechnology applications. The NCL recently completed its first year of operation and is actively characterizing nanoparticles for academic and commercial researchers through a rigorous set of analytical protocols. The NCL works closely with the National Institute of Standards and Technology (NIST) and the U.S. Food and Drug Administration (FDA).
- **Multidisciplinary research training and team development** is a major focus of the Alliance because the application of nanotechnology to cancer challenges requires teams of scientists with knowledge and understanding that crosses disciplines, particularly in the biological and physical sciences. The Alliance will

support training and career development initiatives to establish integrated teams of cancer researchers. The Alliance will provide this training support through existing and new mechanisms. For example, the Alliance will provide training funds through the NIH National Research Service Awards for Senior Fellows and the NIH National Research Service Awards for Postdoctoral Fellows. In addition, in September 2005, through the NCI's collaboration with the National Science Foundation (NSF), $12.8 million in new grants were awarded to four institutions over the next 5 years for U.S. science and engineering doctoral students to focus on interdisciplinary nanoscience and technology research with applications to cancer (see NCI-NSF press release, September 21, 2005).

## CANCER NANOTECHNOLOGY PLATFORM PARTNERSHIPS

A key component of the NCI's Cancer Nanotechnology Plan is to fund the development of technology platforms that offer opportunities for advances in the near- and medium-terms and that lower the barriers for those advances to be developed by the private sector into a new generation of diagnostic and therapeutic products. Each of the Cancer Nanotechnology Platform Partnerships will focus on meeting this goal through directed research projects with specific products as deliverables.

Modeled after the successful NIH Bioengineering Research Partnership, each award represents a strong combination of technical and oncology expertise that will utilize a wide range of nanotechnologies in their efforts to address six specific areas of emphasis:

- Molecular Imaging and Early Detection
- *In Vivo* Nanotechnology Imaging Systems
- Reporters of Efficacy
- Multifunctional Therapeutics
- Prevention and Control
- Research Enablers

In making the Cancer Nanotechnology Platform Partnership awards, the NCI is recognizing the scientific merit and clinical promise of the research projects, as well as the strength of the multidisciplinary teams, which include researchers from the public and private sectors that have come together to participate in these Alliance programs. The teams associated with each of the Platform Partnerships will engage in directed, product-focused research that will aim to translate cutting-edge science and technology into the next generation of diagnostic and therapeutic tools that will ultimately benefit cancer patients.

Nanotechnology represents a wide range of scientific endeavors and tools, and the awards reflect that broad cross-section of technologies and disciplines being applied by teams distributed geographically across the United States, with applications across the entire spectrum of cancers and cancer patients. The selected Platform Partnerships will engage in a range of near-term projects that are approaching clinical use, as well as cutting-edge

projects that will have an exceptionally significant impact on clinical oncology if they are brought to fruition.

**Nanotherapeutic Strategy for Multidrug-Resistant Tumors**

This partnership, which includes researchers from Northeastern University, the Roger Williams Medical Center, Massachusetts General Hospital, and Massachusetts Institute of Technology, will develop multifunctional targeted nanoscale devices to deliver therapeutic agents and tumor resistance modulators directly to cancer cells as a means of overcoming multiple-drug resistance. Preliminary work by this team has already produced biodegradable, tumor-targeted drug nanocarriers, and this team is now ready to begin translational efforts to move this research along a development path to the clinic.

The initial oncology focus of this project will be breast and ovarian cancers. Team members have expertise in nanoparticle design, pharmaceutical chemistry, cancer biology, and clinical oncology.

Statement from principal investigator Mansoor Amiji, Ph.D., Northeastern University

*"Getting this award is very exciting because we now have a real opportunity to develop nanoparticle systems that will overcome the problem of multiple-drug resistance that develops in a large percentage of tumors. This award allows us to assemble the team of basic and applied scientists and physicians that we need to put together all of the pieces that we've developed over the past few years into a biocompatible nanoparticle package that we can begin testing in animals, and hopefully then in humans."*

Mansoor M. Amiji, Ph.D.
Associate Professor, Pharmaceutical Sciences, School of Pharmacy
Bouve College of Health Sciences
Northeastern University

**DNA-linked Dendrimer Nanoparticle Systems for Cancer Diagnosis and Treatment**

As an offshoot of work initiated under the NCI's Unconventional Innovations Program, this partnership at the University of Michigan will develop multi-component, dendrimer nanoparticles that will target, image, and treat cancer. This partnership will first refine technology designed to assemble the various dendrimer components into a multifunctional device, and then begin preclinical testing of the resulting formulations. This partnership will make extensive use of the NCI's Nanotechnology Characterization Laboratory (NCL) to generate the preclinical safety and pharmacokinetic data needed to move these nanoparticles to the clinic.

Team members have expertise in dendrimer development, immunology, cancer biology, and clinical oncology. The initial focus of this project will be epithelial tumors.

Statement from principal investigator James Baker, Jr., M.D., University of Michigan

*"This funding allows us to develop a platform that could revolutionize cancer therapy by providing personalized molecularly assembled drugs. Our prior work has demonstrated the feasibility of this concept, yielding prototypes that could be in the clinic within one year."*

James Baker, Jr., M.D.
Ruth Dow Doan Professor
Professor of Internal Medicine
Director, Michigan Nanotechnology Institute for Medicine & Biological Sciences
University of Michigan

**Metallofullerene Nanoplatform for Imaging and Treating Infiltrative Tumor**

This partnership at the Virginia Commonwealth University will develop metal-based fullerenes (buckyballs), a type of hollow, spherical nanoparticle, to simultaneously deliver imaging agents and anticancer therapeutics to brain tumors known as gliomas. The initial oncology focus of this project will be brain cancer, and team members have expertise in experimental and clinical imaging, chemistry, neurosurgery, oncology, and tumor targeting. Metal-based fullerenes were invented by one of the partnership team members.

Statement from principal investigator Panos Fatouros, Ph.D., FACR, Virginia Commonwealth University

*"By using metal-based fullerenes known as 'buckyballs' to deliver imaging agents and therapeutic agents into the brain, we are gaining the ability to visualize and treat lethal types of brain cancer. This NCI platform award will accelerate our efforts to exploit the novel attributes of these nanomaterials and translate them into effective products to overcome some of the most intractable challenges faced in oncology today."*

Panos Fatouros, Ph.D., FACR
Professor of Radiology
Chair, Division of Radiation Physics & Biology, Department of Radiology
Virginia Commonwealth University

**Detecting Cancer Early with Targeted Nano-Probes for Vascular Signatures**

This project intends to develop highly specific molecular imaging probes that will enable non-invasive early detection of incipient cancer, affording substantive improvements in sensitivity and selectivity. It brings together three research groups with complementary expertise, in angiogenesis and mouse models of cancer (Douglas Hanahan, UCSF), in vascular profiling (Erkki Ruoslahti, Burnham Institute), and in clinical and experimental molecular imaging (Ben Franc, UCSF). The team will utilize peptides that specifically home through the circulatory system to find "zip codes" on the angiogenic blood or

lymphatic neo-vasculature of high-grade neoplasias and/or invasive carcinomas. These vascular signatures can distinguish cancerous lesions from their cognate normal tissue, as well as from blood/lymphatic vessels in other organs and other neoplastic conditions. In addition some peptides can distinguish premalignant from malignant lesional stages. By linking these signature-finding peptides for vascular zip codes to both traditional and investigational imaging agents, the group will produce modular molecular probes for early detection of cancer. These targeted probes for neoplastic vascular signatures will serve as platforms for testing the benefits of new nanotechnology-based imaging agents with improved properties (e.g., higher signal output) forthcoming from the new Centers of Cancer Nanotechnology Excellence and the Cancer Nanotechnology Platform Partnership programs.

Statement from principal investigator Douglas Hanahan, Ph.D., UCSF Comprehensive Cancer Center, UCSF Diabetes Center

*"I and my collaborators, Drs. Ruoslahti and Franc, are excited about the potential to apply nanotechnologies to cancer detection and therapy. We foresee the identification of 'zip codes' of the angiogenic blood and lymphatic vessels of tumors will facilitate the specific delivery of modular nano-probes aimed to more accurately detect and/or destroy human tumors, involving powerful new nanoscale technological agents to be developed by the NCI's Cancer Nanotechnology Platform Partnerships."*

Douglas Hanahan, Ph.D.
Professor, Biochemistry
University of California at San Francisco
UCSF Comprehensive Cancer Center (Program leader, Mouse Models of Cancer Program)
UCSF Diabetes Center (Member)

**Photodestruction of Ovarian Cancer: ErbB3 Targeted Aptamer-Nanoparticle Conjugate**

This partnership at the Massachusetts General Hospital is focused on developing multifunctional nanoparticles that can deliver light-activated anticancer compounds specifically to ovarian cancer cells. Once bound to the target cells, the nanoparticles are activated using a miniature endoscopic laser to illuminate only the tumors, providing a second means of ensuring that healthy tissue is spared damage during therapy. The partnership team members have expertise in photodynamic therapy, fiber-optic procedures, and nanoparticle design and synthesis.

Statement from principal investigator Tayyaba Hasan, Ph.D., Massachusetts General Hospital and Harvard Medical School

*"The nanotech platform partnership award is a very exciting opportunity to work collaboratively with investigators at Brigham and Women's Hospital and the Department of Pathology at the Massachusetts General Hospital toward developing a new optical*

*approach for the treatment of ovarian cancer. The prognosis for women diagnosed with ovarian cancer remains poor — less than a third will survive 5 or more years — and such new treatment approaches are imperative.*

*"The program envisions a selective, externally activated therapy involving nanoparticles conjugated to aptamers which target ovarian cancer cell and deliver high payloads of light activatable molecules in an emerging modality called photodynamic therapy (PDT). Among advantages of PDT, the two most notable are the dual selectivity inherent in the method and its reported effectiveness on cells that have become resistant to chemotherapeutic agents."*

Tayyaba Hasan, Ph.D.
Professor of Dermatology, Wellman Center for Photomedicine
Director, Office of Research Career Development
Massachusetts General Hospital and Harvard Medical School

**Hybrid Nanoparticles in Imaging and Therapy of Prostate Cancer**

This partnership at the University of Missouri-Columbia, will use its established expertise in nanomaterial design to create gold nanoparticles capable of imaging molecular abnormalities associated with the earliest stages of prostate cancer. By incorporating gold nanoparticles on cancer specific peptides, the partnership's investigators hope to create agents that can both image and treat small prostate tumors. Team members, who will be able to draw upon a substantial infrastructure funded by the University of Missouri to accelerate their translational efforts, have expertise in chemistry, radiology, veterinary sciences, pathology, physics, and biocompatible nanoparticle development.

Statement from principal investigator Kattesh Katti, Ph.D., University of Missouri-Columbia

*"Putting together a good, strong group of researchers with the expertise we needed for this project was a challenge, but it was well worth it because we got some great ideas out of the process. Now, we're all ready to go. We're all ready to see if we can exploit the unique properties of nanoparticles, exploit the discoveries we've made in terms of how to create biocompatible nanoparticles, and actually put our discoveries and ideas to the test with a focused goal of developing nanoparticles for imaging and treating prostate cancer in humans."*

Kattesh Katti, Ph.D.
Professor of Radiology & Physics
Senior Research Scientist MU Research Reactor
University of Missouri-Columbia

## Near-Infrared Fluorescence Nanoparticles for Targeted Optical Imaging

This partnership, a collaboration between the researchers at The University of Texas M. D. Anderson Cancer Center and Eastman Kodak, aims to develop novel nanoparticles for targeted molecular optical imaging of early-stage tumors. The fluorescent nanoparticles, developed at Kodak, emit near-infrared fluorescence light that can penetrate deep into tissues. The nanoparticles will be targeted to tumor-associated antigens, reporting their presence or absence in the tumors. Nanoparticles are also designed to respond to enzymatic action which light up only when first activated by enzymes found exclusively on the surface of certain types of cancer cells. The partnership will focus on studies to fully characterize the biological behavior of these particles and target them to a wide variety of cancer cells.

The initial oncology focus of this project will be brain, breast, and skin cancers. Team members have expertise in nanoparticle formulation, imaging science, neurosurgery, and molecular biology.

Statement from principal investigator Chun Li, Ph.D., The University of Texas M. D. Anderson Cancer Center

*"Engineering nanometric particles to fully realize their potential in anticancer diagnosis and therapy represents the cutting-edge research in functional nanomaterials. Optical imaging is a highly sensitive method that can detect minute amounts of light-emitting materials. The NCI grant allows us to systematically study the pharmacologic properties of near-infrared light-emitting nanoparticles based on Kodak's platform technology. Information on the fundamental interplay between the nanoparticle's physicochemical properties and their in vivo fate will be dissected and used to design nanoparticles that will one day be used to detect cancers at an early stage and to detect the response of tumors to treatment."*

Chun Li, Ph.D.
Associate Professor, Experimental Diagnostic Imaging
The University of Texas M. D. Anderson Cancer Center

## Integrated System for Cancer Biomarker Detection

This partnership at the Massachusetts Institute of Technology (MIT) will develop microfluidic devices whose nanochannels are capable of concentrating rare proteins from biospecimens. These devices will then be integrated with another chip-based device to detect and quantify panels of proteins that may serve as early signs of cancer. The devices will be fabricated in such a way as to enable widespread and low-cost distribution for use in the healthcare setting. The initial oncology focus of this project will be prostate cancer, and team members have expertise in nanofabrication, clinical oncology, and cell biology.

Statement from principal investigator Scott Manalis, Ph.D., Massachusetts Institute of Technology

*"The timing for this award couldn't be better because we are ready to go with our technology. We are ready to solve the hard problems that remain for us to create a clinically useful fluidics device that will impact medicine in a real way.*

*"I think that the milestones and performance metrics built into these awards are very important because what we're doing is certainly product oriented, and metrics are important for developing technology effort."*

Scott Manalis, Ph.D.
Associate Professor of Biological and Mechanical Engineering
Massachusetts Institute of Technology

**Novel Cancer Nanotechnology Platforms for Photodynamic Therapy and Imaging**
This partnership, which includes team members from the Roswell Park Cancer Institute, the University of Buffalo, and the University of Michigan, will develop targeted nanoparticle platforms for detecting and imaging cancers, and selectively delivering light-activated anticancer compounds for guided photodynamic therapy (PDT). Because of the team's extensive experience with the systems they are developing — previous work was funded in part by NCI's Unconventional Innovations Program — this partnership expects to validate the usefulness of their nanoparticles both for imaging tumors and then killing them with PDT, using models for breast, lung, prostate and colon cancers. Partnership team members have expertise in nanoparticle design, animal models of human cancer, photodynamic therapy, imaging, and clinical oncology.

Statement from principal investigator Allan Oseroff, M.D., Ph.D., Roswell Park Cancer Institute and University at Buffalo School of Medicine and Biomedical Sciences

*"Nanotechnology platforms offer the unique opportunity to package large numbers of tumor-seeking photodynamic therapy drugs together with sensitive imaging agents. Our group's goal is to develop these novel targeted nanoparticles for a 'see-and-treat' approach that will selectively eradicate cancerous lesions in patients."*

Allan Oseroff, M.D., Ph.D.
Chairman, Departments of Dermatology
Roswell Park Cancer Institute
and University at Buffalo School of Medicine and Biomedical Sciences

**Multifunctional Nanoparticles in Diagnosis and Therapy of Pancreatic Cancer**
Investigators from the State University of New York at Buffalo and Johns Hopkins School of Medicine have combined forces in this partnership to develop and test multifunctional, hybrid ceramic-polymeric nanoparticles that will deliver imaging and

therapeutic agents to pancreatic tumors. This group has a strong history of developing novel, biocompatible nanomaterials — including non-toxic quantum dots — that have the capacity to be targeted to specific types of cancer cells. Based on the prior work by members of this partnership, they expect to begin translating their work into preclinical and clinical studies in the near-term. Partnership team members have expertise in materials design and clinical oncology.

Statement from principal investigator Paras Prasad, Ph.D., University at Buffalo

*"Our receipt of this award is a demonstration of the significant scientific results we have achieved, applying our nanoparticles to critical applications in diagnosing and treating cancer. We are very excited to be working with our Johns Hopkins colleagues in a project designed to accelerate nanotechnology's move out of the laboratory and into the cancer clinic."*

Paras Prasad, Ph.D.
Distinguished Professor of Chemistry
University at Buffalo

**Nanotechnology Platform for Targeting Solid Tumors**

This program at the Sidney Kimmel Cancer Center will build on extensive experience in nanoparticle development and blood vessel biology to create nanodevices that will target specific cells lining blood vessels in order to improve transit out of the bloodstream and into tumors. Miniaturized probes can be injected into the bloodstream to go throughout the body and not only report back the state of each organ, but actually seek out and treat cancer. This technology has application for imaging and therapy of a wide variety of solid tumors, both primary and metastatic (or disseminated disease) including breast, prostate, kidney, colon, and lung. The team is a collaboration at the Sidney Kimmel Cancer Center that includes chemists, molecular imagers, tumor biologists, and molecular biologists.

Statement from principal investigator Jan Schnitzer, M.D., Sidney Kimmel Cancer Center, San Diego

*"Nanomedicine has the potential to provide new treatments and even cures for many diseases. But its complexity requires the interaction of many fields of science, from chemistry to physics to biology to clinical medicine. All must work cooperatively and learn each other's 'language' to create new, effective, and biocompatible nanoparticles that can revolutionize medicine and cancer treatment as we know it today."*

Jan Schnitzer, M.D.
Scientific Director and Director of Vascular Biology and Angiogenesis Program
Cellular and Molecular Biology Program
Sidney Kimmel Cancer Center, San Diego

**Nanotechnology Platform for Pediatric Brain Cancer Imaging and Therapy**
A collaborative effort among researchers at the University of Washington, the Fred Hutchinson Cancer Research Center, Children's Hospital and Regional Medical Center, and Philips Medical Systems, this partnership team will develop imaging agents and multifunctional nanoscale drug delivery vehicles targeted to medulloblastoma, the most common brain tumor in children. This partnership will focus on building on its previous research and developing translational efforts to bring this technology into the clinic. The partnership team members have expertise in pediatric brain cancer, tumor molecular biology, magnetic resonance imaging, and materials science.

The principal investigator is Raymond Sze, M.D., University of Washington.

*"Pediatric brain cancers are the most common solid malignancies in children. Although survival has improved, frequently the end result of the current chemotherapy and radiation therapy regimens is a significant loss of neurocognitive potential. In surgery, an important determinant of prognosis is complete tumor resection, yet brain cancer tissue looks very similar to surrounding normal brain. The surgeon is therefore in the difficult position of balancing risk from leaving residual cancer tissue with resection of normal tissue with vital function. Our nanotechnology platform represents an attempt to significantly improve diagnosis and treatment, as well as long-term survival and preservation of neurocognitive function, in this most common of pediatric solid tumors."*

Raymond Sze, M.D.
Associate Professor of Radiology
Research Affiliate, Center on Human Development and Disability
University of Washington

**ABOUT THE NCI ALLIANCE FOR NANOTECHNOLOGY IN CANCER**
To help meet the goal of eliminating suffering and death due to cancer, the National Cancer Institute is engaged in efforts to harness the power of nanotechnology to change the way we diagnose, treat, and prevent cancer. The NCI Alliance for Nanotechnology in Cancer is a comprehensive, systematized initiative encompassing the public and private sectors, designed to accelerate the application of the best capabilities of nanotechnology to cancer. Among the Alliance goals are to develop research tools to identify new biological targets, as well as agents to monitor predictive molecular changes in order to prevent precancerous cells from becoming malignant. In addition, the Alliance promotes the development of better diagnostics and treatment regimens using nanotechnology to target specific cancer cells amongst healthy cells.

The Alliance for Nanotechnology in Cancer is an integrated, milestone driven, and product-oriented program with targeted objectives and goals, initiated to capitalize on opportunities to create the tools that both clinicians and cancer researchers need now to eliminate suffering and death due to cancer. By working to fulfill this core mission of the NCI, the Alliance offers training and career development mechanisms to direct talent to

this area as quickly as possible and to incentivize cross-disciplinary research through training the scientific community. For more information on the NCI Alliance for Nanotechnology in Cancer, please visit http://nano.cancer.gov/.

**ABOUT THE NATIONAL CANCER INSTITUTE**

The National Cancer Institute (NCI) is a component of the National Institutes of Health (NIH), one of eight agencies that compose the Public Health Service (PHS) in the Department of Health and Human Services (DHHS). The NCI, established under the National Cancer Act of 1937, is the Federal Government's principal agency for cancer research and training. For more information about the NCI, please visit http://www.cancer.gov/.

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